

LISTING OF CLAIMS

Please amend the claims as follows. This listing of claims will replace all prior versions and listings of claims in the application.

1. (Cancelled)
2. (Currently Amended) A variant antithrombin III, comprising a substitution at position P3, wherein the substitution at P3 is ~~a-D~~, an E, H, K, L, P, Q, R, W, or Y.
3. (Withdrawn) A variant antithrombin III, comprising a substitution at position P4, wherein the substitution at P4 is a L, N, Q, or V.
4. (Currently Amended) A variant antithrombin III, comprising one substitution at either position P3 and P4, wherein the substitution at P3 is ~~D~~, an E, H, K, L, P, Q, R, W, or Y, and wherein the substitution at P4 is L, N, Q, V, or W, and at least one substitution at P2, P5, P6, P7, and P8, wherein the substitution at P2 is P, P5 is E, F, G, or P, wherein the substitution at P6 is E, G, L, or T, wherein the substitution at P7 is E or Q, and wherein the substitution at P8 is E.
5. (Currently Amended) A variant antithrombin III, comprising two substitutions at P3 and P4, wherein the substitution at P3 is ~~D~~, an E, G, H, I, K, L, N, P, Q, R, S, W, or Y, and wherein the substitution at P4 is L, N, Q, V, or W.
6. (Currently Amended) A variant antithrombin III, comprising two substitutions at either position P3 and P4, wherein the substitution at P3 is ~~D~~, an E, H, K, L, P, Q, R, W, or Y, and wherein the substitution at P4 is A, F, G, L, N, P, Q, V, or W.
7. (Currently Amended) A variant antithrombin III, comprising two substitutions at P2, P3 and P4, wherein the substitution at P2 is P, wherein the substitution at P3 is ~~D~~, an E, G, H, I, K, L, N, P, Q, R, S, W, or Y, and wherein the substitution at P4 is A, F, G, L, N, P, Q, V, or W.

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8. (Currently Amended) A variant antithrombin III, comprising a substitution at P2, P3 and P4, wherein the substitution at P2 is P, wherein the substitution at P3 is ~~D~~, an E, H, K, L, P, Q, R, S, W, or Y, and wherein the substitution at P4 is L, N, Q, V, or W.

9. (Currently Amended) A variant antithrombin III, comprising one substitution at P3 and P4, wherein the substitution at P3 is ~~D~~, an E, H, K, L, P, Q, R, S, W, or Y, and wherein the substitution at P4 is L, N, Q, V, or W, and wherein P2 is P.

10. (Withdrawn) A variant antithrombin III, comprising one substitution at P5, wherein the substitution at P5 is D, H, N, Q, R, S, T, V, W, or Y.

11. (Withdrawn) A variant antithrombin III, comprising one substitution at P7, wherein the substitution at P7 is F, H, L, S, T, or V.

12 – 28 (Cancelled)

29. (Original) The variant ATIII of claims 1-20, wherein the variant ATIII has a combined activity greater than or equal to plasma ATIII in a coupled assay.

30. (Original) The variant ATIII of claim 29, wherein the ATIII retains base thrombin inhibition activity of at least 5%.

31 – 32 (Cancelled)

33. (Original) The variant ATIII of claim 29, wherein the the variant ATIII produce a predicted half life of thrombin at 60 minutes after a bolus administration to a subject that is greater than or equal to .9 the half life following a plasma ATIII administration.

34 – 38 (Cancelled)

39. (Original) The variant antithrombin III of claim 29, wherein the variant antithrombin III has an increased protease resistance greater than or equal to the protease resistance of plasma ATIII.

40. (Currently Amended) The variant antithrombin III of claim 29, wherein the variant antithrombin III has an increased human ~~neutrophil~~ neutrophil elastase resistance greater than

or equal to the protease resistance of plasma ATIII.

41. (Original) The variant antithrombin III of claim 29, wherein the variant antithrombin III has an increased cathepsin G resistance greater than or equal to the protease resistance of plasma ATIII.

42. (Cancelled)

43. (Original) The variant ATIII of claims 1-20, wherein the variant ATIII retains increased protease resistance and retains observable anti-thrombin activity.

44 - 50

51. (Original) The variant ATIII of claims 1-20, wherein the variant ATIII retains increased protease resistance and retains observable anti factor fXa activity.

52 – 60 (Cancelled)

61. (Currently Amended) A method of inhibiting septic disseminated intravascular coagulation in a subject comprising by administrating the an ATIII variant of claims 1-20 to a subject having septic disseminated intravascular coagulation, wherein the ATIII variants inhibit thrombin, thereby inhibiting septic disseminated intravascular coagulation in the subject.

62. (Currently Amended) A method of reducing sepsis in a subject, comprising administering the an ATIII variant of claims 1-20 to a subject having sepsis, thereby reducing sepsis in the subject.

63. (Currently Amended) A method of inhibiting sepsis induced shock in a subject comprising administering the an ATIII variant of claims 1-20 to a subject, thereby reducing sepsis induced shock in the subject.

64. (Cancelled)

65. (Original) A method of making the variant ATIII of claims 1-20, comprising linking in an operative way a nucleic acid molecule encoding a protein set forth in SEQ ID NO:77 wherein the nucleic acid sequence comprises a sequence that hybridizes under stringent

hybridization conditions to a sequence set forth SEQ ID NO:79, or a degenerate variant thereof, and a sequence controlling the expression of the nucleic acid.

66. (Original) A cell comprising the variant ATIII of claims 1-20.

67. (Withdrawn) A non-human animal comprising the variant ATIII of claims 1-20.

68 – 70 (Cancelled)

71. (Original) A cell produced by the process of transforming the cell with any of the disclosed nucleic acids of claims 64 or 65.

72. (Original) A cell produced by the process of administering the variant ATIII of claims 1-20.

73. (Withdrawn) A non-human animal produced by administering any of the variant ATIIIs of claims 1-20.

74. (Withdrawn) A non-human animal produced by administering the cell of claim 73.